

We Claim:

1. A composition comprising a submicron oil-in-water emulsion, and a selected antigen entrapped in,
5 or adsorbed to, a biodegradable microparticle.

2. The composition of claim 1, wherein the microparticle is formed from a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide),
10 poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

3. The composition of claim 2, wherein the microparticle is formed from poly(D,L-lactide-co-glycolide).
15

4. The composition of claim 1, wherein the submicron oil-in-water emulsion comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®, and optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine.
20

5. The composition of claim 1, wherein the selected antigen is a viral antigen.
25

6. The composition of claim 5, wherein the selected antigen is gp120.

7. The composition of claim 5, wherein the selected antigen is p24gag.
30

8. The composition of claim 5, wherein the selected antigen is hepatitis C virus E2.

9. The composition of claim 1, wherein the selected antigen is entrapped in the microparticle.

10. The composition of claim 1, wherein the
5 selected antigen is adsorbed to the microparticle.

11. A composition comprising (a) a submicron oil-in-water emulsion which comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®, and
10 optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine, and (b) a selected antigen entrapped in, or adsorbed to, a poly(D,L-lactide-co-glycolide microparticle.

15 12. The composition of claim 11, wherein the selected antigen is entrapped in the microparticle.

20 13. The composition of claim 11, wherein the selected antigen is adsorbed to the microparticle.

14. A method of immunization which comprises administering to a vertebrate subject (a) a submicron oil-in-water emulsion, and (b) a therapeutically
25 effective amount of a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle.

15. The method of claim 14, wherein the microparticle is formed from a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide),
30 poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

16. The method of claim 15, wherein the microparticle is formed from poly(D,L-lactide-co-glycolide).
35

17. The method of claim 14, wherein the submicron oil-in-water emulsion comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®,
5 and optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine.

18. The method of claim 14, wherein the
10 selected antigen is a viral antigen.

19. The method of claim 18, wherein the selected antigen is gp120.

20. The method of claim 18, wherein the
15 selected antigen is p24gag.

21. The method of claim 18, wherein the selected antigen is hepatitis C virus E2.
20

22. The method of claim 14, wherein the selected antigen is entrapped in the microparticle.

23. The method of claim 14, wherein the
25 selected antigen is adsorbed to the microparticle.

24. The method of claim 14, wherein the submicron oil-in-water emulsion is administered prior to the microparticle.
30

25. The method of claim 14, wherein the submicron oil-in-water emulsion is administered subsequent to the microparticle.
35

26. The method of claim 14, wherein the submicron oil-in-water emulsion is administered substantially concurrently with the microparticle.

5 27. A method of immunization which comprises administering to a vertebrate subject the composition of claim 11.

10 28. A method of making a composition comprising combining a submicron oil-in-water emulsion with a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle.

15 29. The method of claim 28, wherein the selected antigen is entrapped in the microparticle.

20 30. The method of claim 28, wherein the selected antigen is adsorbed to the microparticle.

25

30

35

40